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Investigation of the practices, legislation, supply chain and regulation of opioids for clinical pain management in Southern Africa: A multi-sectoral, cross-national, mixed methods study

Eve Namisango, MSc, Matthew J. Allsop, BSc, PhD, Richard A. Powell, BA, MA, MSc, Stefan J. Friedrichsdorf, MD, FAAP, Medical Director, Emmanuel BK. Luyirika, Fatia Kiyange, BA, MA, MPH, Edward Mukooza, MBchB, MBL, PGDPH, Chris Ntege, Pharm, Bsc MPSU, Eunice Garanganga, BSc, MSc, Dip palliative care, Dip Midwifery, RN, Mavis Ntombifuthi Ginindza – Mdluli, BSc, Msc, Faith Mwangi-Powell, MSc Econ, PhD, Lidia Justino Mondlane, Bsc, Msc, PhD, Richard Harding, BSc, MSc, DipSW, PhD

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Investigation of the practices, legislation, supply chain and regulation of opioids for clinical pain management in Southern Africa: A multi-sectoral, cross-national, mixed methods study

Eve Namisango*[1], Matthew J Allsop[2], Richard A Powell[3], Stefan J. Friedrichsdorf [4] Emmanuel BK Luyirika[1], Fatia Kiyange[1], Edward Mukooza[5], Chris Ntege[6], Eunice Garanganga[7], Mavis Ntombifuthi Ginindza – Mdluli , Faith Mwangi-Powell[3], Lidia Justino Mondlane[9], Richard Harding[9]

* = corresponding author

- Eve Namisango (MSc): [1]African Palliative Care Association, P.O. Box 72518, Plot 850 Dr Gibbons Road, Kampala, Uganda and King's College London, Cicely Saunders Institute, London, UK; eve.namisango@africanpalliativecare.org
- Matthew J Allsop (BSc, PhD): [2]Leeds Institute of Health Sciences, University of Leeds, Leeds, UK; m.j.allsop@leeds.ac.uk
- Richard A. Powell (BA, MA, MSc): [3]MWAPO Health Development Group, P.O. Box 459-00621, Village Market, Nairobi, Kenya; richard2powell@yahoo.co.uk
- Stefan J. Friedrichsdorf (MD, FAAP) Medical Director, [4]Department of Pain Medicine, Palliative Care and Integrative Medicine, Children's Hospitals and Clinics of Minnesota, Associate Professor of Pediatrics, University of Minnesota, Minneapolis, MN, USA

Opioid analgesia in three Southern Africa countries

- Emmanuel BK Luyirika: [1]African Palliative Care Association, PO Box 72518, Plot 850 Dr Gibbons Road, Kampala, Uganda; emmanuel.luyirika@africanpalliativecare.org
- Fatia Kiyange (BA, MA, MPH): [1]African Palliative Care Association, PO Box 72518, Plot 850 Dr Gibbons Road, Kampala, Uganda; fatia.kiyange@africanpalliativecare.org
- Edward Kibikyo Mukooza (MBchB, MBL, PGDPH): [5]Uganda Christian University, Box 4, Mukono, Uganda; mukooza_edward@yahoo.com
- Christopher Ntege B (Pharm, Bsc MPSU): [6]Hospice Africa Uganda, Kampala, Uganda; ntegechris@gmail.com
- Eunice Garanganga (BSc, MSc, Dip palliative care, Dip Midwifery, RN): [7]Hospice & Palliative Care Association of Zimbabwe, 13 Lezard Avenue, Milton Park, Harare. Zimbabwe. eunice@hospaz.co.zw
- Mavis Ntombifuthi Ginindza – Mdluli (BSc, Msc): [8]Ministry of Health, P.O. Box 5, Mhlambanyatsi Road, Mbabane, Swaziland. ntombiginindza@yahoo.com
- Faith Mwangi–Powell (MSc Econ, PhD): [3]MWAPO Health Development Group, P.O. Box 459-00621, Village Market, Nairobi, Kenya.
- Lidia Justino Mondlane (Bsc, Msc, PhD): [9]Mozambique Palliative Care Association, Av. EmÃlia DaÃºsse, 382. Mozambique. lmonjane@yahoo.ca
- Richard Harding (BSc, MSc, DipSW, PhD): [10]King's College London, Cicely Saunders Institute, London, UK. richard.harding@kcl.ac.uk

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Abstract

Context: Sub-Saharan Africa faces an increasing incidence and prevalence of life-limiting and life-threatening conditions. These conditions are associated with a significant burden of pain linked to high morbidity and disability that is poorly assessed and undertreated. Barriers to effective pain management partly relate to lack of access to opioid analgesia and challenges in their administration.

Objectives: To identify country-specific and broader regional barriers to access, as well as the administration of opioids, and generate recommendations for advancing pain management in Southern Africa.

Methods: A parallel mixed methods design was used across three countries: Mozambique, Swaziland and Zimbabwe. Three activities were undertaken: (i) a review of regulatory and policy documentation; (ii) group interviews, and; (iii) a self-administered key informant survey.

Results: Barriers to accessing opioid analgesics for medical use include: overly restrictive controlled medicines' laws; use of stigmatizing language in key documents; inaccurate actual opioid consumption estimation practices; knowledge gaps in the distribution, storage and prescription of opioids; critical shortage of prescribers, and; high out-of-pocket financial expenditures for patients against a backdrop of high levels of poverty.

Conclusion: Policies and relevant laws should be updated to ensure the legislative environment supports opioid access for pain management. Action plans for improving pain treatment for patients suffering from HIV or non-communicable diseases should address barriers at the different levels of the supply chain that involve policymakers, administrators and service providers.

Keywords

Opioids, analgesia, pain, supply chain, Africa, palliative care

Running title: Opioid analgesia in three Southern Africa countries

Introduction

Pain and symptom control are necessary for quality palliative care delivery in sub-Saharan Africa (SSA)[12]. Pain is the commonest symptom experienced by those with the two most prevalent life-limiting and life-threatening conditions managed by palliative care services in the region: HIV and cancer[28,34]. For HIV, pain prevalence has been reported in 54 - 83% of patients [13,33], typically associated with sensory neuropathy, a common manifestation among HIV patients on antiretroviral therapy (ART)[36,38]. For cancer, pain prevalence is reported between 39 – 66%, dependent on disease stage [50]. The global burden of HIV and cancer (specifically infection-related) both disproportionately affect SSA [32,43]. Of the 36.7 million people globally living with HIV[48], 70% live in SSA[47]. The prevalence of cancers are rising, too[56], with an expectation that non-communicable diseases (NCDs) will be the lead cause of mortality in developing countries by 2030[37,52].

Palliative care improves pain management (e.g., through the provision of pain medication) for patients and their families [8,14,16] and patient survival[2,41]. However, for palliative care and pain treatment strategies to be effective, they must be incorporated by governments into all levels of their health care systems[6]. Effective pain management is subject to the availability of appropriate medicines, policies, educational frameworks and evidence[40]. For example, the World Health Organization (WHO) recommends morphine as the primary analgesic for the treatment of moderate-to-severe pain [9,57,58]. Consumption of morphine in SSA is low, with large proportions of SSA patients enduring untreated pain[31]. Recently the International Narcotics

Control Board (INCB) and WHO have encouraged governments to evaluate their healthcare systems, laws and regulations, and identify and remove impediments to the availability of controlled substances for medical needs[20]. Global policy and legal frameworks exist to remove avoidable suffering among patients with advanced disease, and promote cheap and effective palliative care as a public health and human right issue [11,26]. However, reports of barriers to the supply and provision of opioids are widespread, highlighting inherent challenges faced in many countries within Africa: over-regulation[4], insufficiently trained clinical personnel to prescribe, cost[31], unreliable supply mechanisms and procurement difficulties[15], and weak health systems[7,31,35]. Countries continue to struggle to strike a balance between effective drug control and facilitating its availability for pain management in clinical practice.

Studies on supply chains in palliative care services have occurred in some SSA regions [24,28], with significant investigation of the factors associated with lack of access [15,28,51]. To date, there has been no systematic assessment of factors affecting the supply and availability of opioids in Southern African countries. This is essential to address shortfalls in opioid supply and clinical use in a region with the highest HIV prevalence in SSA[48] and where unrelieved cancer pain is a significant problem[3]. This study aimed to identify country-level and regional specific factors relevant to the supply and availability of opioid analgesics for medical use in three countries in the region.

Methods

Study setting and design

A convergent parallel mixed methods design was used[5]. Three activities were undertaken: (i) a desktop review of regulatory and policy documentation; (ii) group interviews, and; (iii) a self-administered questionnaire among purposefully sampled key personnel involved in opioid regulation and clinical service providers. The self-administered questionnaire sought information from respondents on their knowledge of, and attitudes to, supply chain issues and estimation practices concerning the availability of opioid analgesics. All data collection tools were pre-tested in Uganda and modified accordingly to ensure clarity of question items. This involved reviewing the tools for appropriateness for purpose based on the objectives, clarity and duration of interviews.

The study covered three countries in Southern Africa: Mozambique, Swaziland and Zimbabwe (characteristics of these countries are outlined in Table 1). We purposively sampled countries at different levels of palliative care development using the Worldwide Palliative Care Alliance Palliative Care Development map[25]. Mozambique is at Level 3a (isolated palliative care provision); Swaziland is at Level 3b (generalized palliative care provision); and Zimbabwe is at Level 4a (hospice-palliative care services are at a stage of preliminary integration into mainstream service provision). This approach enabled the identification of gaps and practices at the three levels of palliative care development in the region. Furthermore, it provides a more representative perspective of service provision in the region.

[Insert Table 1 about here]

(i) Desktop documentation review

To identify policy-level barriers to opioid access and availability, a desktop review of national regulatory and policy documents relevant to governing the use of controlled medicines – and specifically opioids – was conducted.

(ii) Group interviews

To understand existing supply chain mechanisms, three group interviews were conducted with key informants knowledgeable about the subject matter in each of the three countries. These discussions were directed by a topic guide informed by the document review and the content of INCB guidelines for the country assessment of national drug control policies[20]. The group interviews sought to explore the following policy- and legislative-level concern: government practices in regard to controlled medicines policies, legislation and regulation. Key issues addressed included: policy-related barriers to access, planning for the availability and accessibility of controlled medicines, estimation procedures, other barriers to accessing opioids for pain management, practices around opioid prescription and dispensing and human resource concerns.

(iii) Key informant survey

A questionnaire with closed-ended questions was developed to assess knowledge and attitudes related to opioid consumption, estimation, manufacturing, importation, distribution, storage, prescription and regulation. Participants provided socio-demographic information and rated their agreement/disagreement with a series of statements in each of the domains using a 5-point Likert scale (i.e., strongly disagree, disagree, uncertain, agree, and strongly agree). Statements were also informed by the INCB guidelines[20]. The assessment of knowledge, attitudes and practices covered three core domains: (i) awareness of governments' responsibility to integrate opioids in relevant national pharmaceutical and disease-specific policies; (ii) knowledge of regulating the distribution, storage and prescription of opioids, and; (iii) attitudes of participants regarding opioid consumption estimates, importation, storage, distribution and prescription. Statements outlined INCB recommended practices on reporting frequency, management of controlled medicine stock, the role of strong opioids in the treatment of pain among patients, and attitudes toward opioid consumption estimation, importation and the manufacturing process.

Sampling and data collection

(i) Desktop documentation review

To identify the scope of documents, we followed existing approaches to identifying health policy and systems relevant documents regarding governing use of controlled medicines[30]. We also reviewed INCB reports and guidelines to identify relevant documents to target. We sought to identify reports, strategies, rapid response

summaries, policy dialogue reports, policies, plans, guidelines and evidence briefs for policy. The list of documents to be reviewed was shared with in country key informants to confirm their comprehensiveness and relevance. These were subsequently reviewed for content to identify barriers and good practices. Documents written in Portuguese were reviewed by the Portuguese speaking policy experts in Mozambique. (LMN and LD)

(ii) Group interviews

Contact persons from national palliative care associations (Mozambique and Zimbabwe) and national Ministries of Health (Swaziland) identifyed and contacted group interview participants. Purposive sampling was used to select officials knowledgeable about the supply chain mechanisms at the different levels of service delivery.. These included representatives from: (i) the country Ministry of Health; (ii) the pharmaceutical department in the medicines regulatory authority; (iii) the Ministry of Internal Affairs, and departments of law enforcement on controlled medicines; (iv) the Central Medical Stores, and; (v) health service delivery facilities. The interviews were conducted by two people (moderator and note taker). Field notes were taken during the interviews catchy quotes were captured verbatim and these were subsequently expanded into transcripts at the end of each day.

(iii) Key informant survey

Sampling for the key informants was undertaken at two levels: (i) purposive sampling of informants from the Medicines Regulatory Authority, with the aim of identifying those

knowledgeable about the subject matter and ensuring representation of the different levels of service delivery; (ii) snowball sampling (i.e., existing study subjects recruited future subjects from among their acquaintances) to identify service providers, using the group interview participants as the index points of contact. Officials who participated in the group interviews were requested to identify service providers within or affiliated to their respective departments to take part in the key informant survey. The service providers were drawn from both public and private facilities, national palliative care associations or palliative care help desks and other related programmes. The questionnaire was distributed to the respective personnel responsible for service provision for self-completion.

Ethical approval to undertake the study was received from the Comité National de Bioética para a Saúde (CNBS) / Mozambique National Committee for Bioethics (reference number 26/CNBS/13, 2014), the Scientific and Ethics Committee of the Ministry of Health in Swaziland (reference number MH/599C/FWA 000 15267, August 2013), and the Medical Research Council of Zimbabwe (reference number MRCZ/A/1800, August 2014). Written informed consent to participate in the study was obtained from all participants.

Data analysis

For the document review, we used the WHO Policy Guidelines for Controlled Substances[55] to develop a template for assessing barriers and good practices in existing policy guidelines. The guidelines outline how to ensure balance in national

policies on controlled substances. All documents were appraised against this template. Good practices and barriers were documented in a summary table followed by content analysis of the data extracted.

Data from group interviews were also analyzed using content analysis. Two data analysts (EN and EM) deconstructed the data manually and categorised and synthesised emergent themes. Texts were broken into segments representing salient concepts and labelled with a code[27,45]. Any discrepancies in the coding were resolved through discussion alongside any subsequent adjustments to coding. Cross-cutting themes were identified and subsequently discussed by the research and in-country teams. SPSS version 16 was used to analyze the quantitative data from the self-administered questionnaires. A descriptive approach was taken, with data summarized by frequencies and proportions.

Results

(i) Desktop documentation review

Documents identified and reviewed included controlled medicines policy documents (n = 4) and regulatory frameworks (n = 11) (see Table 2).

[Insert Table 2 about here]

Identified potential barriers to opioid access included stigmatizing language, lack of balance when negotiating avoidance of illicit opioid use and access for medical use, and overly restrictive prescription practices:

- It was common for legal documents to contain stigmatising terms such as "dangerous drugs", "dangerous substance", for example in the *Dangerous Drugs Act (Chapter 15:02) of Zimbabwe*
- Overly restrictive practices in prescribing were also noted in the policy document contents, with doctors as the main legal prescribers. For example, in the *National Palliative Care Trainees Manual (2013)* for Swaziland, it is stated on page 81 that "Legislation on morphine use: Morphine is a controlled … class C drug in Swaziland. Prescribed by authorized clinicians – doctors"
- National guidance favors availability of controlled medicines at higher levels of service delivery, such as hospitals, while not being available at primary health care level
- Documents often do not accommodate the concept of balance, encouraging access to opioid analgesics for medical and scientific use while ensuring that diversion or illicit use of opioids is minimized. For example, *Mozambique's Criminal Jurisdiction Legal Framework Applicable to Trafficking and Consumption Narcotic Drugs, Psychotropic Substances, Precursors and other Substances Similar Effects Law No 3/97*, dated 13 September 1997. Objectives of this law focus on the control of illicit use of controlled substances and in the Act there is no mention of the need for the use of controlled substances for scientific and medical purposes to control moderate to severe pain.
- Mozambique is yet to achieve the milestone of embedding morphine in the national essential medicines list (i.e. medically necessary medicines that should

be provided in sufficient quantities, as unavailability would cause serious harm). Swaziland and Zimbabwe already have essential medicines lists[10,59], which include morphine as an essential medicine, that should be made available to all those in need.

While potential barriers were identified, cross-cutting themes reflecting best practices also emerged. All three countries have designated authorities responsible for overseeing the importation, production, sale and distribution of controlled medicines. They also all have some form of policy guidelines to guide the delivery of palliative care services and regulate access to opioids for pain management.

(ii) Estimation procedures and supply chain mechanisms

In total, 33 participants (including government policy, licensing, supply chain and law enforcement personnel, National AIDS Program / palliative care associations and national palliative care coordination desks) participated in group interviews.

[Insert Table 3 about here]

These thematic issues are presented in Table 4 by country and explained below.

[Insert 4 about here]

Estimation procedures used for determining the need for opioids was consumption based across all three countries. This involves using previous consumption data to predict future need, which consequently guides the amounts imported for medical use. The burden of disease and total population are not used in these calculations:

"In estimating for opioids need in Zimbabwe, past consumption is the main factor we consider. The burden of disease or total population is never included, so we cannot prevent shortages before the year ends. For example, in 2012, the case estimated amount was not sufficient, so a supplementary estimate was sent to INCB." Group Interview ID 04, Zimbabwe

Countries tried to include a 10% surplus in these estimates to prevent shortages before the year ends. In situations where the estimated amount was insufficient, supplementary estimates were sent to the INCB. All countries reported frequent stock-outs (ranging from 50% of the time in Zimbabwe, to 80% in Mozambique). None of the countries mentioned using the integrated approach of combining consumption with morbidity data as recommended by the INCB[21].

Stock outs of opioids were common and attributed to delays in the tendering process and scarcity of resources, particularly US dollars, required for the importation and distribution of opioids:

"Stock outs are very common here and this is due to several things. There are delays in the tendering process; also scarcity of resources is a problem, particularly dollars, required for the importation and distribution of opioids." Group Interview ID 02, Mozambique

Delays in mandatory reporting to the INCB were also mentioned in Swaziland as a challenge at the time of data collection:

"The government has not submitted to the INCB the required quarterly and annual statistical reports because of the lack a technical person to take on this role for the last five years; this technical officer had just been recruited and hired in 2014." Group Interview ID 10, Swaziland

Several barriers to accessing opioids were also identified; these include the impact of distance to the nearest health facility and service availability, restrictive prescription privileges (only allowing morphine to be supplied on prescription at hospital sites), and rural-urban imbalances to pain management services (limited health worker numbers and stock in rural facilities). The rural-urban imbalances in access were exacerbated by the restrictive prescription practices which favour doctors who are mostly urban based:

"The inadequacy of health worker numbers and the fact that morphine is only available in hospitals, where there were doctors to prescribe it, is also a limiting factor. Lack of

access is worse in rural areas which have fewer hospitals and fewer doctors". Group Interview,ID 09 Mozambique

"Pharmacies are mostly located in towns and liquid morphine is not easily accessed by users in rural areas. Prescription is restricted to registered doctors, most of whom are urban based so rural-urban imbalance in access is a problem". Group Interview, 011 Swaziland.

User fees at the point of service delivery were in operation in the three countries and cited as a potential barrier to those who may not be able to afford these costs:

"In Mozambique, there is a user fee of 5 metical [equivalent to about 17 US cents] at the point of access, there is a waiver for the very poor and those with chronic diseases but it is still a barrier." Group Interview ID 01, Mozambique

"There is a user fee of 10 emalangeni (equivalent to about US$1) at the point of access, after which all services and medicines could be accessed. It is a problem to some patients." Group Interview ID 05, Swaziland

"Although Zimbabwe has a user fee policy, treatment for HIV and AIDS was supposed to be free; in reality; there is high out-of-pocket expenditure because essential medicines were not always available in public health facilities and patients have to buy

them from the open market. This increases costs for all health services, including palliative care and access to opioid analgesics." Group Interview ID 06, Zimbabwe

Group interview participants also highlighted several policy-level issues within existing policy documents that needed review to improve access to opioids for pain management.

"Regarding regulation and legislation of the pharmaceutical industry in Swaziland, the current National Pharmaceutical Policy (2011c) states on page 11 that "The Pharmacy Act of 1929" … is outdated, does not provide for licensing … and regulatory functions … licensing of premises and registration of medicines is not done." Group Interview ID 06, Swaziland

"We have the Dangerous Drugs Act (Chapter 15:02) it should be revised to accommodate the concept of 'balance' and not focus only on the prevention of the illicit use of opioids. In this way, it will create an environment for supporting availability and access for the rational medical and scientific use of opioids". Group Interview ID 09, Zimbabwe

(iii) Key informant survey

Characteristics of key informants

In total, 88 participants from Mozambique (n = 26), Swaziland (n = 30) and Zimbabwe (n = 32) completed the key informant survey (see Table 5). Nearly two-thirds of

respondents were female, with 51.1% nurses and 20.4% non-medical professionals. Just over half (51.1%) identified themselves as a 'service provider'.

[Insert Table 5 about here]

Knowledge, attitudes and practices regarding opioid analgesic supply, distribution and storage

The level of awareness of governments' responsibility to integrate opioids in relevant national pharmaceutical and disease-specific policies was generally good (i.e. scores are above 70% for knowledge about: the role of government in opioid regulation-need to have policy guidance on opioid regulation, need for moderate/severe pain management beyond cancer and supply chain requirements for controlled medicines). The role of government was deemed critical to improving opioid availability by ensuring controlled medicines are stocked like other medicines. Respondents were generally aware that HIV/AIDS may be associated with pain. The proportion of respondents who agreed/strongly agreed that physicians, nurses and other health professionals who are trained and qualified, at all levels of health care should be allowed to prescribe ranged between 33%-64%. Notably, the majority of respondents were more inclined towards very stringent measures regarding storage and prescription. Regarding estimation, importation and distribution, there was very low knowledge among respondents (see Table 6). The knowledge and attitudes on other domains highlighted areas that may require strengthening (i.e. less than 70% of respondents or more chose the correct option).

[Insert Table 6 about here]

Respondents generally had accurate knowledge regarding collaboration of their countries with the INCB (range for agree/strongly agree scores 67%-100%). However, awareness of the respondents' countries being signatories to international drug control conventions was generally low across the three countries (range 53%-61%).

Integration and synthesis of findings and proposal for future initiatives

Drawing on the synthesis of findings from the mixed methods study, we propose context-specific approaches to improve the supply and subsequent clinical use of opioids in Southern Africa in response to issues identified in this study. Proposed approaches are outlined in Figure 1, describing issues and approaches for each level of the opioid supply chain.

[Insert Figure 1]

Discussion

This study presents evidence on the processes and systems surrounding opioid availability in three Southern African countries. We propose context-specific solutions in response to issues identified that could be useful in improving access to opioids for pain management in the Southern Africa region. Findings from this review of policy and regulatory documentation revealed countries trying to institute appropriate policies and guidelines. While these have been developed across all three countries between 2011 and 2014, barriers remain, including the use of stigmatizing language which may contribute to the fear of using opioid medicines and be associated with restrictive access [51]. Controlled medicine laws should not aim at diminishing access to opioid medicines for medical use but rather strengthen it. To strike a balance, the laws/policies should support optimization of safety whilst minimizing risk, avoiding negative consequences that could result from diversion or unintentional overdose. A lack of balance could ultimately have an impact on access to opioids for medical use both at the supply and prescription levels.

Current opioid estimation practices do not mirror recommended best practices, which involve use of both consumption and disease incidence data[20,21]. Failure to follow these practices results in a significant gap between the number of deaths and those where analgesic treatment was available. This may partly explain the high percentage of unmet pain treatment needs reported in Mozambique, Swaziland and Zimbabwe[44]. Furthermore, the escalating incidence of cancer and other NCDs could contribute to a widening of the gap between the amount of medication available for pain relief and the

amount needed[19,55]. The need to revise estimation procedures should be a high priority.

There were cases where countries had not submitted INCB reports for some time. This finding echoes increasing reports of countries not submitting estimates for their controlled substances based upon careful assessment of population needs to the INCB, as required by the UN drug conventions[18]. This could explain why opioid consumption levels for pain treatment have increased in other parts of the world except in Asia, Africa and Middle Eastern countries[20]. The INCB has repeatedly reminded countries of their obligation to submit estimates based upon population need and has encouraged all countries to review their methods for preparing estimates to ensure they reflect the need for controlled medications[21]. The staff in charge of estimation and reporting in INCB procedures should be trained and mechanisms instituted to provide the data required for making estimations that incorporate disease burden. In 2016, the INCB launched the Learning project, to provide technical assistance to member states to improve compliance with international drug control convention provisions. Through this initiative a series of three-day regional training seminars have been held for national authorities responsible for the implementation of the international drug control conventions, which included training on estimates. These were held in 2016 and 2017 in East Africa, South and East Asia, and Europe[49]. We recommend that the INCB considers holding a Southern Africa regional training seminar.

At the supply level, cost also affects the availability of opioids. Frequent stock-outs of opioids was highlighted as a common challenge and their causes were partly related to lack of financial resources to import opioid analgesics. Mozambique is a low-income country with a per capita income of US$ 600, while in Zimbabwe 72% of the population live below the poverty line[42]. Amidst a chronic lack of financial resources, countries are encouraged to create capacity for the local production of basic oral morphine, in tablet or liquid form, at low cost[17]. While the sustainability of such services requires consideration, a number of countries have successfully initiated this approach[26]. At the patient level, some countries charge user fees as a strategy for leveraging resources to sustain the services, particularly in situations where government funding is deemed inadequate. Under the right to health, governments do not have to offer medications, such as oral morphine, free of charge. However, they must strive to ensure they are affordable to all[18].

Restrictive prescription privileges continue to be a barrier to opioid medicine access, with prescribing mainly restricted to doctors in Mozambique and Swaziland. This finding further contributes to the converging evidence on inadequate health care resources, including health care professionals, as a barrier to access[20]. The restrictive prescription practices have important implications for the region given critical shortages of health workers, especially doctors, the commonest prescribers, with a failure to comply with the WHO 2.28/1000 (health worker to population) recommendation[53]. This is a serious concern for a region characterized by limited access to trained doctors, and an escalating burden of HIV and NCDs[46]. Integral to the concern of human

resource shortage is the significant inequitable distribution of health workers in urban versus rural areas [39]. The availability of prescribers is skewed towards urban settings in situations where currently only doctors are allowed to prescribe opioid analgesics. These prescribers are also more likely to be stationed at urban-based secondary or higher levels of service delivery. With the majority of the population living in rural areas, patients may have to travel long distances to access prescription points. This problem raises a multitude of concerns in terms of equitable access to opioid medicines for pain relief.

The conventional doctor-led model in opioid medicine prescription may be justifiable because of the complexity involved in their handling and prescription. Nevertheless, innovation is urgently needed to address associated challenges faced in African settings. The WHO recommends re-structuring health service models to accommodate task shifting as a way of solving acute human resource for health shortages[54]. Task shifting involves transferring specific tasks to different cadres of health workers with shorter training experience and fewer qualifications. It may also include delegation of specified duties to cadres who receive targeted training to acquire a specific set of skills [23]. Notably, the definition of the various cadres of non-physician health workers differs from country to country[29], making country-specific plans important in rolling out this agenda. For example, Hospice Africa Uganda currently provides a course for nurse prescribers, preparing them for the prescription role. This corresponds to high-resource countries like the USA, where nurse-practitioners can prescribe opioids in many

states[1]. Evidence for effectiveness of the task shifting of this role is urgently needed to support its role out in the field of opioid medicine prescription in the region.

Globally, there is an enormous, increasing gap between the need for, and availability of, opioid analgesics, and this is increasingly skewed against people living in poverty[22]. For Southern African countries,

Conclusion

Numerous barriers to effective pain management have been identified across legislation, supply and clinical use of opioids in three Southern African countries. In response to barriers identified in this work we present recommendations for future initiatives to enhance pain management that are specific to the Southern African context. However, these have relevance to palliative care providers across the SSA region. Recommendations require adaptation to the local country in which they are implemented alongside research activities to explore their effectiveness. Recommendations include advocacy for policy changes, revisions to prescribing restrictions, exploring the scope for local opioid morphine production, reducing user fees, and addressing knowledge gaps at the level of policy, government and health professionals. Pursuing these initiatives, influencing all levels of the opioid supply chain, aim to improve the management of pain for patients suffering with progressive disease and reduce the extensive avoidable suffering reported in this region.

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Fig. 1: Overview of opioid supply chain levels with identified issues and proposed context-specific approaches to aid improvement

Table 1: characteristics of these three Sub-Saharan African countries

Description	Mozambique	Swaziland	Zimbabwe
Population (in million) 2015 [1]	27.98	1.27	15.6
Gross national income (GNI) per capita (US$) 2012 [3]	510	2860	680
Children 0-14 years 2015 [1]	45.3%	37.3 %	41.6 %
Life expectancy at birth (years) 2012	49.9	48.9	56.1
Annual number of under-5 deaths (thousands) 2012 [3]	84	3	39
Adult HIV prevalence (%) 2012 [3]	11.1	26.5	14.7
Children living with HIV (thousands) 2012 [3]	180	22	180
Cancer mortality (2012) [4]	17,017	628	11,423
Total amount of morphine equivalent consumed in 2012	4.7kg	Not reported	10.1kg
Morphine needed to meet minimum demand from deaths due to HIV or cancer (kg)	177kg	20kg	322kg
Deaths with moderate/severe pain	52,114	3,252	28,638
People dying of HIV or cancer with untreated moderate/severe pain:	51,348	3,252	27,001
Based on morphine equivalent consumed, coverage of deaths in pain with treatment	1.5%	0.0%	5.7%
Percentage gap in coverage of deaths in pain with analgesics treatment:	98.5%	100%	94.3%

Data from (1) http://data.worldbank.org (2015); (2) http://www.painpolicy.wisc.edu/countryprofiles (3)

https://www.unicef.org/infobycountry/zimbabwe_statistics.html [4] http://globocan.iarc.fr/Pages/summary_table_pop_sel.aspx

[5] Treat the Pain (2014)

Table 2: Documents reviewed for each country and comments on the documents

Country	Policies	Regulatory frameworks and other relevant documents identified	Comments on documents
Mozambique	• Palliative Care National Policy of 2012:12	• Criminal Jurisdiction Legal Framework Applicable to Trafficking and Consumption Narcotic Drugs, Psychotropic Substances, Precursors and other substances Similar Effects Law No. 3/97, dated 13 September 1997 • African Palliative Care Association (ACPA) Standards for Providing Palliative Care in Africa (2011). These were (adopted by Mozambique in 2012) • Pocket Guide to Pain Management 2nd Edition (2012). Adopted from APCA and translated into Portuguese. • National Formulary Medicines	• There are several documents that refer to palliative care and opioids. • Effects Law No 3/97, dated 13 September 1997, which has been superseded by events and does not match or meet the current situational needs. This law was enacted in 1997 and has not been revised to address changes in disease epidemiology; for example, escalating incidence and prevalence of cancer, HIV and other NCDs for which pain is a highly prevalent symptom. This moderate/severe pain is best managed using opioids to reduce unnecessary suffering. This law is still in effect in Mozambique. • The National Strategic HIV and AIDS Response Plan 2010–2014, does not address issues of pain management and only briefly mentioned palliative care under the home-based care section.
Swaziland	• National Palliative Care Policy (Ministry of Health, 2011) • National pharmaceutical policy (2011)	• National Palliative Care Trainees Manual (2013) • Curriculum for pharmacy certificate program (no date) • Standard Treatment Guideline and Essential Medicines List of Common Medical Conditions in the Kingdom of Swaziland (2012) • Swaziland Pharmaceutical Strategic Plan of 2012-2016 (Ministry of Health, 2012a)	• Swaziland's 1929 Pharmacy Act and 1922 Opium and Habit Forming Drugs Act were long outdated; as they do not provide for licencing and regulatory functions. Two new bills (a Pharmacy Bill of 2012 and a Medicines Bill of 2012) are yet to be enacted into law, for now the existing acts are still in effect. • Swaziland's Pharmaceutical Strategic Plan for 2012–2016, page 17, the opioids are listed as essential medicines. • The Pharmaceutical Policy of 2011 talks about control (Article 6.2.2) as well as the supply of all essential medicines (Article 6.3). • The National Palliative Care Guidelines (MoH Swaziland, 2011a:15) state that "morphine is the most commonly used opioid and is still the absolute standard".

Country	Policies	Regulatory frameworks and other relevant documents identified	Comments on documents
Zimbabwe	• The National Medicines Policy (2011)	• Dangerous Drugs Act (Chapter 15:02) of Zimbabwe • The Medicines and Allied Substances Control Act (Chapter 15:03) of 1969 • National HIV and AIDS strategic plan (2011)	• The Dangerous Drugs Act (Chapter 15:02) does not accommodate the concept of 'balance' to enhance availability of opioids for rational medical and scientific use of opioids. • In the National Medicines Policy of Zimbabwe (MOHCW, 2011), opioids are classified as vital drugs but with 'B' availability –, these medicines can only be stocked at hospital level. • The Medicines and Allied Substances Control Act (Chapter 15:03) of 1969 established the Medicines Control Authority of Zimbabwe (MCAZ), which controls the manufacturing, import/export and distribution of medicines, including opioids. • As per the National Health Strategy of Zimbabwe 2009–2013 page 9), access to all essential drugs was not good, ranging between "29% and 58% for vital items-including opioids, and 22% to 36% for all items". • There is a national HIV and AIDS Strategic Plan for 2011–2015 (National AIDS Council of Zimbabwe, 2011), which states that palliative care is one of the services to be provided under community-based health care (CBHC), with a goal to scale it up to 85% by 2015. • As per the National Medicines Policy (Ministry of Health and Child Welfare, 2011) government is obliged to provide 'vital' medicines including opioids. • The national HIV and AIDS Strategic Plan for 2011–2015 (National AIDS Council of Zimbabwe, 2011), states that palliative care is one of the services to be provided under community-based health care (CBHC), with a goal to scale it up to 85% by 2015.

Table 3: Participants recruited to the study (n=121)

Group Interview participants (n=33)							
Country	***Informant category***						
	National AIDS Program/ palliative care association	Government Policy Personnel	Government Licensing Personnel	Government Supply chain personnel	Service Providers	Law enforcement Personnel	**Total number**
Mozambique	4	4	1	1	1	0	**11**
Swaziland	4	2	1	0	4	0	**11**
Zimbabwe	1	2	1	1	5	1	**11**
Total	*9*	*8*	*3*	*2*	*10*	*1*	***33***
key informant questionnaire (n=88)							
Country	***Informant category***						
	National AIDS Program/ palliative care association	Government Policy Personnel	Government Licensing Personnel	Government Supply chain technocrats	Service Providers	Law enforcement Personnel	**Total number**

Mozambique	2	3	1	0	20	0	**26**
Swaziland	3	8	5	0	9	5	**30**
Zimbabwe	7	1	1	2	16	5	**32**
Total	*12*	*12*	*7*	*2*	*45*	*10*	***88***

Table 4: Gaps in Controlled medicines practices around estimation, prescription and dispensing in patient care

Mozambique	Swaziland	Zimbabwe
Supply related challenges at national level		
• Estimation is based previous year's consumption alone a method likely to under estimate actual need. + • Stock outs were common and largely attributed to the bureaucratic tendering process. • Morphine is imported using foreign currency which is scarce, compromising importation and distribution.	• Estimation is based previous year's consumption alone a method likely to under estimate actual need. + • Irregularities mentioned in submitting reports to the International Narcotics board, yet Non-compliance to reporting can compromise supply. • Human resource shortage concerns were commonly mentioned and linked to irregularities in submitting INCB reports	• Estimation is based previous year's consumption alone a method likely to under estimate actual need. +
Barriers at service delivery level		
Mozambique	Swaziland	Zimbabwe
• Proximate to services access centers as morphine is not available at primary health care level which is closer to the communities' residential areas. • Restrictive prescription regulations (only doctors are allowed to prescribe) • lack of critical mass for prescribers • User fees is a barrier to access for the poor	• Proximity to services; rural vs urban imbalance in service access points. • Restrictive prescription regulations (only doctors are allowed to prescribe) • Lack of critical mass for prescribers • User fee of $1 is a barrier at the point of access	• Proximity to services, there are long distances to service delivery centres as morphine is not stocked at primary health care level. • There is a rural vs urban imbalance as prescribers and services centres are largely urban based in service access points • Frequent stock outs of opiods • User fee at the point of service access is a barrier

+ Morbidity data and the population size are not used in estimating need

Table 5: Characteristics of questionnaire respondents (n=88)

Characteristic		Country			Total
		Mozambique (n=26)	***Swaziland (n=30)***	***Zimbabwe (n=32)***	***n = 88***
Sex	Male	9 (36%)	15 (50%	8 (25%)	32 (36.4%)
	Female	17 (64%)	15 (50%)	24 (75%)	56 (63.6%)
Age category (years)	*≤ 30*	8 (16%)	5 (16%)	3 (9%)	16 (18.2%)
	31 – 40	5 (19%)	12 (40%)	8 (25%)	25 (28.4%)
	41 – 50	9 (35%)	8 (27%)	13 (41%)	30 (34.1%)
	≥51	4 (15%)	5 (17)	8 (25%)	17 (19.3%)
Profession	Physician	1 (4%)	5 (16%)	3 (9%)	9 (10.2%)
	Nurse	14 (54%)	14 (47%)	17 (53%)	45 (51.1%)
	Pharmacist	7 (27%)	2 (7%)	7 (22%)	16 (18.2%)
	Non-medical	4 (15%)	9 (30%)	5 (15.6%)	18 (20.4%)
Last time in pain management training	<1yr	7 (27%)	13 (43%)	14 (44%)	34 (39%)
	1-5 yrs.	10 (39%)	9 (30%)	9 (28%)	28 (32%)
	>5yrs	9 (34%)	5 (17%)	4 (13%)	18 (20%)
	Do not know	0	3 (10%)	5 (15%)	8 (9%)
Role in opioids availability	Policy formulation	3 (11%)	8 (27%)	1 (3%)	12 (13.2%)
	With palliative care program	2(8%)	3 (10%)	7 (22%)	12 (13.2%)
	Licensing Authority	1(4%)	1 (3%)	1 (3%)	3 (3.4%)
	Service provider	20 (77%)	9 (30%)	16 (50%)	45 (51.1%)
	Law enforcement	0	5 (17%)	5 (16%)	10 (11.4%)
	Other	0	4 (13%)	2 (6%)	6 (6.8%)

Table 6: Knowledge attitudes and practices regarding opioid analgesic supply, distribution and storage

		Doctors and pharmacists (n=25)	Nurses (n=45)	Non-medical (n=18)
	Awareness on national collaboration with INCB requirements			
1	My country is signatory to the international drug control conventions.	***15(60.0%)***	***24(53.3%)***	***11(61.1%)***
2	Government is required to submit quarterly and annual statistical reports on import and exports.	21(84.0%)	***31(68.9%)***	13(72.2%)
3	The WHO has model drug lists of essential medicines which includes opioid analgesics.	22(88.0%)	36(80.0%)	13(72.2%)
4	It is the Government's obligation, in collaboration with the International Narcotics Control Board (INCB), to ensure that opioid analgesics are adequately available.	24(96.0%)	35(77.8%)	***12(66.7%)***
5	INCB recommends that member countries develop a tailored practical method, through national competent authorities, to select, quantify, procure, store, distribute and use controlled medicines including opioid analgesics.	22(88.0%)	***31(68.9%)***	14(77.8%)
6	In a case of underestimation of controlled medicines, the Government has the option of submitting supplementary estimates to the INCB.	20(80.0%)	***31(68.9%)***	13(72.2%)
	Awareness of governments' responsibility to integrate opioids in relevant national pharmaceutical and disease specific policies			
7	Government should include the availability and accessibility of controlled medicines, including opioids, for all relevant medical uses in their national pharmaceutical policy plans.	22 (88%)	40 (88.9%)	14 (77.8%)
8	Access to, and availability of, strong opioid analgesics should be included in specific national disease control programs, such as that of HIV and AIDS and cancer	20 (80%)	38 (84.4%)	15 (83.3%)
9	Similar to any other medicine, controlled medicines need to be in stock in order for it to be continuously	23 (92%)	41 (91.1%)	13 (72.2%)

		Doctors and pharmacists (n=25)	Nurses (n=45)	Non-medical (n=18)
	available for prescription when needed.			
	Knowledge on regulating the distribution, storage and prescription of opioids			
10	To avoid illicit use, controlled substances availability should only be limited to hospital or large pharmacies with stringent safety measures. **	***5 (20.0%)***	***15 (33.3%)***	***2 (11.1%)***
11	Very stringent safety measures regarding storage of opioids are required to: ensure prevention of diversion, improve availability and affordability of controlled medicines. **	***1 (4.0%)***	***1(4.0%)***	***5 (28.8%)***
12	The INCB recommends that for a pharmacy to be allowed to stock controlled medicines, such as opioid analgesics, they must first invest in additional safety measures to ensure safety of the medicines.	***3 (12.0%)***	***2 (4.4%)***	***1 (5.5%)***
13	There is need to review control and safety measures and the impact on controlled medicines pricing	19 (76.0%)	41 (91.1%)	15 (83.3%)
14	End stage AIDS patients may suffer from pain which may require use of strong opioids analgesics for pain control.	22 (88.0%)	38 (84.4%)	16 (88.9%)
15	Physicians, nurses and other health professionals who are trained and qualified, at all levels of health care should be allowed to prescribe.	***10 (40.0%)***	***29 (64.4%)***	***6 (33.3%)***
16	Medical prescription of opioids for pain control should only be for a limited time. **	***11 (44.0%)***	***28 (62.2%)***	***7 (38.9%)***
17	To be eligible to receive opioids analgesics, patients must be specifically registered and authorized.	***5 (20%)***	***15 (33.3%)***	***2 (11.1%)***
	Attitudes of participants regarding opioid consumption estimates, importation, storage, distribution and prescription			
18	To prevent diversion and illicit use, only government should estimate, import, store and distribute opioid analgesics. **	***9 (36.0%)***	***16 (35.5%)***	***4 (22.2%)***

		Doctors and pharmacists (n=25)	Nurses (n=45)	Non-medical (n=18)
19	Government's main obligation is to ensure that controlled medicines, such as opioid analgesics, are not diverted for illicit use.	***8 (32.0%)***	***5 (11.1%)***	***0 (0%)***
20	Stores or pharmacies to be certified for storage of opioids must, in addition to usual requirements, must have additional specific security.	***2 (8.0%)***	***4 (8.9%)***	***0 (0%)***
21	To ensure prevention of abuse and illicit use, the distribution of controlled medicines including opioids should not be combined with that of other non-controlled medicines distribution systems. **	***6 (24.0%)***	***9 (20.0%)***	***1 (5.6%)***
22	Only pharmacies and hospitals should be permitted to dispense controlled medicines. **	***12 (48.0%)***	***14 (31.1%)***	***5 (27.8%)***
23	Only medical doctors and pharmacists should be allowed to prescribe opioid analgesics. **	***11 (44.0%)***	***22 (48.9%)***	13 (72.2%)

Key: *In italics* = scores <70% (indicating an undesirable score); % = proportion of responses with agree/strongly agree; items with ** = % proportion of responses with disagree/strongly disagree

Levels of opioid supply chain	Barriers identified	Proposed solutions
INCB	• Incomplete and erroneous reporting received	• Provision of training and support to ensure adequate opioid reporting is achieved at the Pharmaceutical Department and Head of the Inspection Unit levels of the supply chain • Hold Southern Africa regional training seminar for national authorities responsible for the implementation of the international drug control conventions, including training on estimates.
Pharmaceutical Department (PD)	• High occurrence of opioid stock outs reported to medicines regulatory authority • Lack of financial resources to import opioid analgesics • Limited data available on burden of disease and opioid prescribing	• Improve access to opioids up to the primary healthcare level by streamlining the supply chain to integrate morphine into the essential medicines list and standard treatment guidelines • Opt for low cost formulations • Provide pharmaceutical opioids management and logistics training to staff in the PD Inspection Unit and the CMS • Facilitate dialogue with PD around reporting on disease burden and opioid prescribing
Head of the Inspection Unit in the PD	• Current estimation procedures are irregular (often completed annually) and rely on consumption data from previous years	• Train key staff in estimation procedures • Strengthen use of data to understand disease burden, which can complement consumption data in opioid needs estimation
Central Medical Store (CMS)	• Frequent occurrence of stockouts of opioids resulting from the tendering process requirements and scarcity of resources (particulary US dollars required for the importation of the opioids)	• Improve access and availability of morphine by providing technical assistance and support towards local manufacturing mirroring initiatives already done in Uganda at Hospice Africa Uganda
Healthcare workforce	• Ratio of doctors within broader healthcare workforce is very low (e.g. in Mozambique there are 34,500 health workers and 3.2% are doctors) • Prescriber reluctant to prescribe due to fear of making mistakes, fear of patient addiction and the additional paper work required • Doctors, the legal prescribers, were mostly urban based and yet most of the population was rural based	• Staff could engage with continued medical education (CME), such as pain management at the clinical level. • Provision of training and education from ministries of health to target identified barriers to opioid prescribing at the healthcare professional level • Ministries of health should evaluate the composition of their healthcare workforce to identify how greater levels of prescribing can be achieved (e.g. increase doctor numbers, authorise additional health professional roles to prescribe) • Ministries of Health should explore ways of reducing or overcoming the urban imbalance of doctors
Service users and caregivers	• User fees exist at at the point of access (e.g. $0.17 in Mozambique) • Average distance moved by service users is about 10 kilometers	• Exemption from fees for the very poor and patients with chronic diseases such as HIV, cancers and TB • Explore innovative approaches to accessing patients to reduce need for travel (e.g. mobile teams from hospice sites, establishing satellite clinics, use of mobile health technology)